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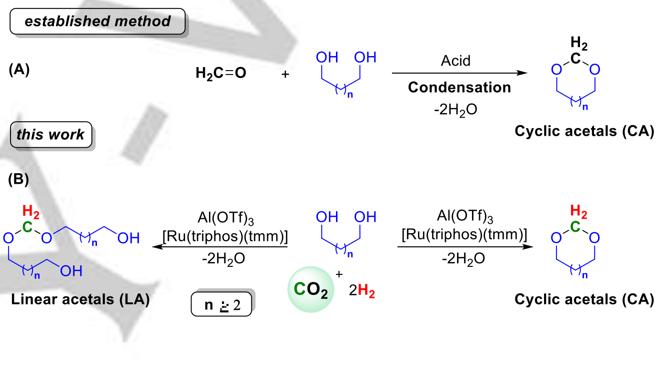
Ruthenium-Catalyzed Synthesis of Cyclic and Linear Acetals via the Combined Utilisation of CO_2, H_2 and Biomass Derived Diols

Kassem Beydoun and Jürgen Klankermayer*[a]

Abstract: Herein a transition metal catalyst system for the selective synthesis of cyclic and linear acetals from the combined utilisation of carbon dioxide, molecular hydrogen and biomass derived diols is presented. Detailed investigations on the substrate scope enabled to largely guide the selectivity of the reaction and demonstrated the possibility to integrate a broad variety of substrate molecules. This approach allowed to change between the favored formation of cyclic acetals and linear acetals, originating from the bridging of two diols with a carbon-dioxide based methylene unit. This new synthesis option paves the way to novel fuels, solvents or polymer building blocks, via the recently established "bio-hybrid" approach, by integrating renewable energy, carbon dioxide and biomass in a direct catalytic transformation.

The catalytic utilisation of carbon dioxide (CO_2) as renewable carbon source enables in principal the optimized synthesis of existing chemical building blocks or the creation of new molecular structures.[1] Furthermore, the increasing availability of non-fossil energy technologies opens unique possibilities to tailor within this concept the interface of energy and material value chains. Conclusively, the incorporation of renewable energy in processes with the combined utilisation of CO_2 and bio-based carbon feedstock offers, in-line with the principles of green chemistry,[2] unprecedented synthetic pathways to carbon reduced fuels, chemicals and solvents, lately introduced as "bio-hybrid" approach.[3]

Recently, a new catalytic reaction provided the first example for such a methodology and demonstrated the selective conversion of CO_2 and renewable hydrogen to the formaldehyde oxidation level.[4] Moreover, when combined with renewable alcohols, this approach opens a novel synthetic pathway to various dialkoxy methane ethers.[4a] The key to this development was the access to a molecular catalyst system with exceptional activity and thermal stability in hydrogenation reactions.[5] In detail, this "bio-hybrid" transformation could be realized with the molecular ruthenium-Triphos catalyst [Ru(triphos)(tmm)] (Triphos=(1,1,1-tri(diphenylphosphinomethyl) ethane, tmm = trimethylene methane) and aluminium triflate ($Al(OTf)_3$) as Lewis acidic co-catalyst, via the formation of methyl formate (MF) and methoxy methanol (MM) intermediates.[4a] Based on this approach the access to a larger family of acetals could be envisaged, thus allowing to substantiate the novel concept. The compounds of great current interest are cyclic acetals (**CA**), such as 1,3-dioxolane, 1,3-dioxane, 1,3-dioxepane. These chemicals represent interesting solvents for numerous applications, as well as important building units for homopolymerization or copolymerization, resulting in polyoxymethylenes as water-soluble polymers.[6] The general and industrially used methodology for the preparation of **CA** is based on the condensation of formaldehyde with glycols in the presence of acidic resin catalysts, affording the corresponding **CA** bearing the 1,3-dioxy moiety (Scheme 1, A).[7]



Scheme 1. "Bio-hybrid" approach towards the synthesis of cyclic acetals **CA** and linear acetals **LA** from the combined utilisation of diols, CO_2 and H_2.

Herein, a novel approach for the synthesis of cyclic acetals **CA** via the utilisation of CO_2/H_2 for the construction of CH_2-unit in combination with various diols is described (Scheme 1, B). Additionally, the molecular catalyst system in combination with selected diols enabled the synthesis of linear acetals **LA**, yielding large diol structures, originating from the bridging of two diols with a carbon-dioxide based methylene unit. These molecules are highly interesting, as they could be utilized as novel monomers for polymerization reactions (Scheme 1, B). Furthermore, the synthesis is adaptable and versatile, as various bio-based diol structures could be utilized.[1, 8] Moreover, the largely different boiling points of the **CA** and **LA** facilitate down-stream processing and separation via distillation.

In the first set of experiments, the [Ru(triphos)(tmm)] complex was investigated in combination with $Al(OTf)_3$ as acidic co-catalyst and 1,3-propanediol as prototypical diol and reaction medium. Generally, the reactions were carried out at a temperature of 80 °C for 18 h with a 1:3 ratio of the CO_2/H_2 gases at a total pressure of 80 bar (pressurized at room temperature) and the TON of the desired product is calculated according to the following equation (n = moles).[4a, 9]

$$TON = \frac{n(acetal)}{n(cat)}$$

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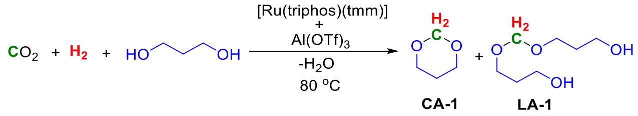
Using the [Ru(triphos)(tmm)] catalyst in 6 µmol and the Lewis acid in 25 µmol resulted in the formation of the envisaged cyclic acetal product 1,3-dioxane **CA-1** with a turnover number (TON) of 32 (Table 1, entry 1). In addition, the unexpected formation of the linear acetal **LA-1** could be identified (TON = 55). This product formally results from the multi-component combination of CO_2, H_2, and two 1,3-propanediol units. Decreasing the catalyst loading to 3 µmol significantly increases the total TON (322) of the acetal products, slightly favoring the **LA-1** product over 1,3-dioxane (Table 1, entry 2). These results clearly indicate that the catalytic system can be optimized by tailoring of the additive to catalyst ratio and catalyst loading.[5a, 10] Moreover, in absence of $Al(OTf)_3$ co-catalyst no acetal products could be detected.

Table 1. Ruthenium-catalyzed synthesis of cyclic acetal **CA-1** (1,3-dioxane) and linear acetal LA-1 using CO_2 and molecular hydrogen.[a]

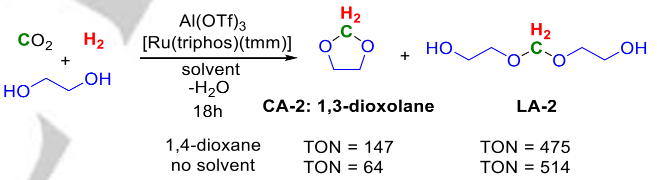


Entry	Solvent/1,3-propandiol	t [h]	CA-1 (TON[b])	LA-1 (TON[b])
1[c]	(--/2)	18	32	55
2	(--/2)	18	137	185
3	DMSO (1/2)	18	13	42
4	2-MeTHF (1/2)	18	71	78
5	THF (1/2)	18	156	125
6	DEE (1/2)	18	121	145
7	1,4-Dioxane (1/2)	18	275	221
8	1,4-Dioxane (1/2)	40	239	100
9[d]	1,4-Dioxane-HCOOH (1-0.2/2)	18	245	179

[a] Reaction conditions: Catalyst = [Ru(triphos)(tmm)] (3 µmol), Acid (25 µmol), 1,3-propandiol (2 mL), CO_2/H_2 (20/60 bar), 18h, 80 °C; [b] Turnover number (TON) was determined by NMR-sepctroscopy using mesitylene as internal standard; [c] [Ru(triphos)(tmm)] (6 µmol); [d] only H_2 (80 bar).

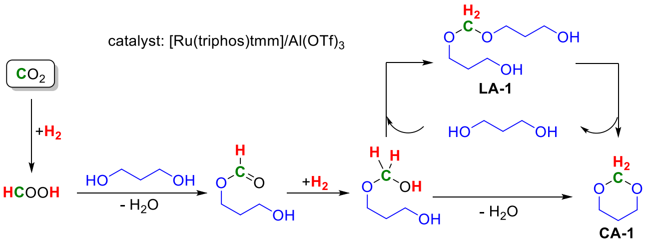
Subsequently, the effect of co-solvents was investigated, as this modification enhances the dissolution of the reactive gases and facilitates reaction control. The use of DMSO resulted in diminished formation of **CA-1** and **LA-1** with minor TONs of 13 and 42 (Table 1, entry 3). Comparable results were obtained with bio-based 2-methyltetrahydrofuran (2-MeTHF) and only TONs of 71 and 78 could be measured (Table 1, entry 4). Using tetrahydrofuran (THF) and diethyl ether (DEE) resulted in the improved formation of **CA-1** with TONs of 156 and 121 and **LA-1** with TONs of 125 and 145 (Table 1, entries 5 and 6). Interestingly, when using 1,4-dioxane as co-solvent, the reaction resulted in the formation of **CA-1** and **LA-1** with an increased TON of 275 and 221 (Table 1, entry 7). This improved reactivity of the catalytic system can be largely attributed to the higher CO_2 solvation capacity of 1,4-dioxane and paves the way to a self-breeding system with the application of the reaction product 1,3-dioxane as solvent.[11] Running the reaction for a longer time (40 h) resulted in increased formation of **CA-1** (TON = 239) and the minor production of **LA-1** (TON = 100), hinting towards a subsequent intramolecular trans-etherification of **LA-1** to **CA-1** (Table 1, entry 8). More detailed information on the optimization of reaction conditions and parameters can be found in the supporting information). Notably, the use formic acid as the C1 source for the construction of the acetal unit in **CA-1** and **LA-1** was investigated and both products were formed in a total TON of 424, slightly favoring the formation of **CA-1** over **LA-1** (TON = 245 and 179, Table1, entry 9).

In the subsequent investigations the influence of diol modifications on activity and selectivity should be evaluated. Consequently, ethylene glycol was used in the standard transformation, resulting in the acetals 1,3-dioxolane **CA-2** and **LA-2** (Scheme 2). **CA-2** is of particular industrial interest, as it represents an important component of industrial polymers and can be used as solvent for polar polymers, leading to applications as cleaner for epoxy and urethane products, where its low boiling point helps achieve high throughput or fast drying.[6] Using the previously optimized reaction conditions, **CA-2** was obtained with a TON of 147 in combination with the major product **LA-2** (TON = 475, Scheme 2). In this transformation the effect of solvent was very pronounced and in a neat reaction mixture increased selectivity towards **LA-2** could be observed (TON = 64 for **CA-2** and TON = 514 for **LA-2**).



Scheme 2. Ruthenium-catalyzed synthesis of 1,3-dioxolane **CA-2** (as a solvent, reagent, or monomer for different polymerization reactions) using ethylene glycol with CO_2 and molecular hydrogen

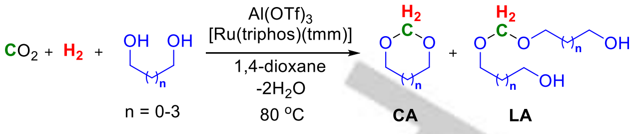
This experimental observation and the comparable results obtained when using HCOOH, lead to the proposal of a sequential pathway for **CA-1** and **LA-1** formation starting from 1,3-propanediol, CO_2 and H_2 (Scheme 3). Thus, HCOOH will be formed via hydrogenation of CO_2, followed by the esterification with 1,3-propanediol, yielding 3-hydroxypropylformate. A subsequent reduction results in the formation of the respective alkoxymethanol intermediate, which is in an intramolecular acetalization reaction forming **CA-1**. In a second pathway, the alkoxymethanol intermediate can be condensed with another 1,3-prapanediol molecule, forming the linear acetal diol product **LA-1**. Importantly, **LA-1** can also serve as an intermediate towards **CA-1** formation via an intramolecular trans-acetalization step, confirmed by the results with increased selectivity at longer reaction times. Thus, a clear difference to the established reaction with formaldehyde is revealed. With respect to the catalysts system, the reduction steps are facilitated by the ruthenium complex, whereas the esterification and acetalization steps are catalyzed by the Lewis-acidity of the multi-functional catalytic system.[12]

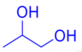
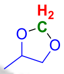
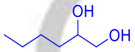
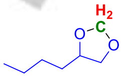
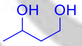
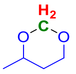
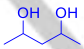
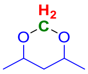
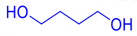
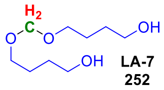
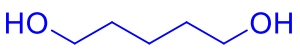
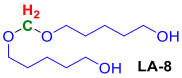
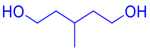
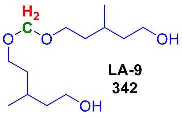


Scheme 3. Reaction pathway for the [Ru(triphos)(tmm)]/Al(OTf)$_3$-catalyzed synthesis of **CA-1** and **LA-1** with 1,3-propanediol.

To evaluate the versatility of this approach for the synthesis of advanced linear and cyclic acetals, the reactivity and chemo-selectivity of reactions with structurally different bio-derived diols was targeted and the decisive experiments are summarized in Table 2. When 1,2-propanediol was used, the transformation afforded 4-methyl-1,3-dioxolane **CA-3** with a TON of 199 as the major product and the linear acetal **LA-3** with a TON of 68, resembling a chemo-selectivity of 74 % (Table 2, entry 1). The use of the sterically more hindered 1,2-hexanediol resulted in a lower overall reactivity towards the acetal products, with 4-butyl-1,3-dioxolane **CA-4** obtained with a low TON of only 38 (Table 2, entry 2). Interestingly, applying 1,3-butanediol, the acetal products were obtained with a total TON of 330 and an astonishing selectivity of 92% towards the 4-methyl-1,3-dioxane **CA-5** in correlation to linear acetal **LA-5** (Table 2, entry 3). Additionally, the use of the sterically more hindered 2,3-pentanediol resulted in the formation of 4,6-dimethyl-1,3-dioxane **CA-6** in a TON of 115 and selectivity of 85% (Table 2, entry 4). Remarkably, the selectivity of the acetal products was significantly reversed when a diol with longer chain was used as substrate. This becomes clearly evident with 1,4-butanediol, affording the linear acetal product **LA-7** as the preferred product with a TON of 252 (86% selectivity, Table 2, entry 5). Furthermore, the use of 1,5-pentandiol and 3-methyl-1,5-pentandiol resulted in a selective formation of the corresponding linear acetal products **LA-8** and **LA-9** with TONs of 151 and 342 respectively (99% selectivity, Table 2, entry 6 and 7) and only trace amounts of the corresponding cyclic acetals were observed. The clearly shifted chemo-selectivity in correlation to the chain length of the applied diols (C2, C3 versus C4, C5) enables to guide the formation of linear and cyclic acetals.

Table 2. Ruthenium-catalyzed selective synthesis of cyclic acetals **CA** and linear acetals **LA** using variable diols with CO$_2$ and molecular hydrogen.[a]



Entry	Diol	Acetal (TON)[b]
1		 **CA-3** **199**
2		 **CA-4** **38**
3		 **CA-5** **305**
4		 **CA-6** **115**
5		 **LA-7** **252**
6		 **LA-8** **151**
7		 **LA-9** **342**

[a] Reaction conditions: [Ru(triphos)(tmm)] (3 µmol), Al(OTf)$_3$ (25 µmol), diol (2 mL), 1,4-dioxane (1mL), CO$_2$/H$_2$ (20/60 bar), 18h, 80 °C; [b] Turnover number (TON) was determined by NMR-spectroscopy using mesitylene as internal standard.

Conclusion

Whereas current approaches largely focus on the combined usage of CO$_2$ and molecular hydrogen towards C1-synthons and e-fuels, the present methodology enables to synthesize complex molecular structures with the additional direct integration of bio-based platform molecules (Figure 1).[13] Thus, the concept of "bio-hybrid" transformations was introduced, envisioning the integration of biomass and CO$_2$ utilization. In the present work a feasibility demonstration was anticipated and in addition to the existing bio-hybrid synthesis of dialkoxy methane ethers,[4a] the catalytic production of versatile linear and cyclic acetals via novel synthetic pathways could be established with TONs up to 622. Moreover, a detailed investigation on the substrate scope enabled to largely guide the selectivity of the reaction and in representative cases a chemo-selectivity >99 % could be achieved. Thus, in these catalytic reactions the versatile catalytic utilization of molecular hydrogen from renewable resources may pave the way to novel processes with largely reduced carbon footprint. Furthermore, the flexibility of the "bio-hybrid" transformations also allows to utilize diols from polymeric waste and research on this topic is currently ongoing in our laboratories.[5c]

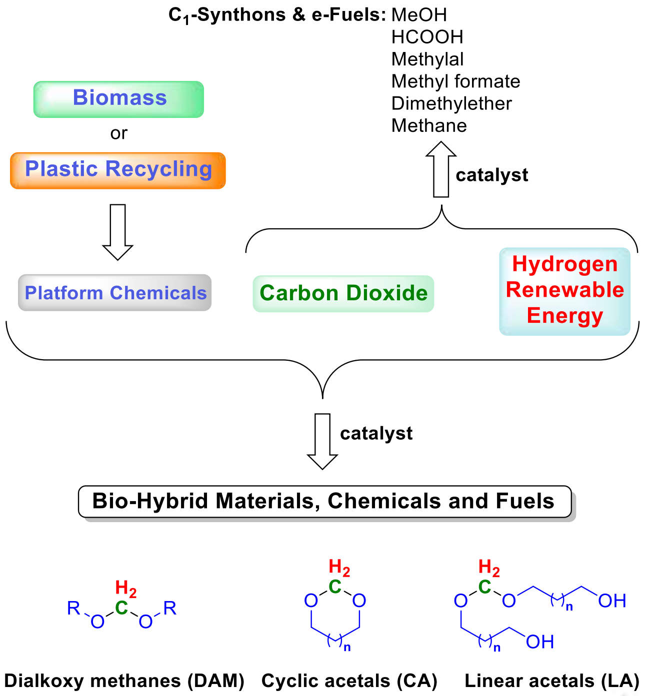


Figure 1. Bio-hybrid approach for incorporation of renewable energy in processes with the combined utilisation of CO_2 and bio-based carbon feedstock.

Experimental Section

General procedure for the synthesis of cyclic acetals (CA) and linear acetals (LA) using diols, CO_2 and H_2: A 2.0 mL solution of [Ru(triphos)(tmm)] (0.002 g, 3 µmol) and $Al(OTf)_3$ (0.012 g, 25 µmol) in the selected diol was prepared under argon atmosphere in a Schlenk tube containing a stirring bar. 1 mL of 1,4-dioxane is added to the solution. After stirring for 5 minutes, the solution was transferred to a carefully degassed and dried 20 mL stainless-steel autoclave. The autoclave was pressurized at room temperature with 20 bar CO_2 and then H_2 was added up to a total pressure of 80 bar. The reaction mixture was stirred with a magnetic stir bar and heated to 80 °C using a preheated aluminum cone. After 18 h the autoclave was cooled in an ice bath and then carefully vented. Turnover numbers (TONs) of desired product in solution were analyzed by 1H-NMR spectroscopy using mesitylene as internal standard with an estimated error of 6%.

Acknowledgements

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Keywords: molecular catalysis · carbon dioxide utilisation · catalytic hydrogenation · sustainable chemistry · green chemistry

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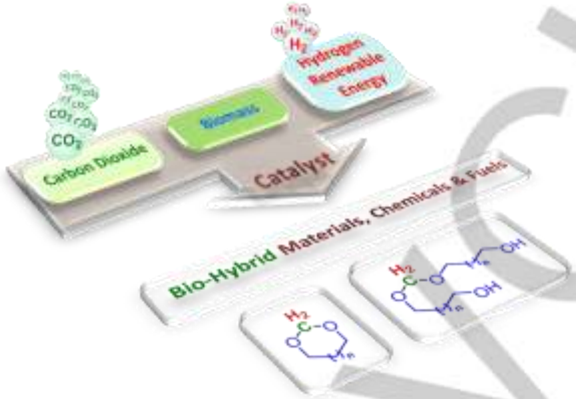
Layout 1:

COMMUNICATION

Bio-hybrid Products: A transition metal catalyst system for the selective synthesis of cyclic and linear acetals from the combined utilisation of carbon dioxide, molecular hydrogen and biomass derived diols is presented. This new synthesis option paves the way to novel fuels, solvents or polymer building blocks, via the recently established "bio-hybrid" approach, by integrating renewable energy, carbon dioxide and biomass in a direct catalytic transformation.



*Kassem Beydoun and Jürgen Klankermayer**

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Ruthenium-Catalyzed Synthesis of Cyclic and Linear Acetals via the Combined Utilisation of CO_2, H_2 and Biomass Derived Diols